UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/030,061	02/25/1998	MATTHEW TODD GILLSPIE	GILLISPIE-1	6893

1444 7590 03/27/2002

BROWDY AND NEIMARK, P.L.L.C.
624 NINTH STREET, NW
SUITE 300
WASHINGTON, DC 20001-5303

EXAMINER
JIANG, DONG

ART UNIT	PAPER NUMBER
1646	15

DATE MAILED: 03/27/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/030,061	GILLSPIE ET AL.	
	Examiner	Art Unit	
	Dong Jiang	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *1/4/2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-6, and 8-28* is/are pending in the application.

4a) Of the above claim(s) *11-27* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6,8-10 and 28* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-6 and 8-28* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED OFFICE ACTION

Applicant's amendment in paper No. 14, filed on 04 January 2002 is acknowledged and entered. Following the amendment, claims 1-3 are amended, and the new claim 28 is added.

Currently claims 1-28 are pending, and claims 1-6, 8-10, and 28 are under consideration.

Double Patenting Rejections:

The rejection of claims 1-5 and 8-10 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 3, and 4 of U.S. Patent No. 6,207,641 B1 is maintained, however, applicants request to hold in abeyance until at least one claim is deemed allowable is acknowledged. Applicants are reminded that at such time, the filing of a terminal disclaimer will overcome the instant rejection. However, Applicants are advised that traversal of the rejection at such time would not be considered timely, and thus, any amendment/argument to the rejection should be addressed in the next response to the present Office Action.

Objections and Rejections under 35 U.S.C. 112:

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-6 and 8-10 remain rejected, and newly submitted claim 28 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, for the reasons cited in the last Office Action, paper No. 12, mailed on 05 July 2001, at pages 4-5.

Applicants amendment and argument, filed on 04 January 2002 (paper No. 14) have been fully considered, but is not deemed persuasive for reasons below.

Applicants amend the independent claim 1 by further defining "functional equivalent". However, the new addition still does not define the term with sequence specificity, therefore, the

metes and bounds of the effective ingredient of the claims still cannot be unambiguously determined.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-3, 5 and 8-10 remain rejected under 35 U.S.C. 112, first paragraph, for lack of enablement (the scope rejection), and lack of written description of "functional equivalents", for the reasons cited in the last Office Action, paper No. 12, at pages 5-7.

Applicants argument in paper No. 14 has been fully considered, but is not deemed persuasive for reasons below.

At pages 6 and 7 of the response, the applicant argues that the term "functional equivalents" is clearly defined in the specification, and that as the amino acid sequences of SEQ ID NO:7 and 6 (mouse and human IL-18, respectively) are provided in the specification, one of skill in the art can readily align the amino acid sequences of human and mouse IL-18, identify sequence conservation, and make the "functional equivalents" based on such guidance taught in the specification. This argument is not persuasive because the main issue is not whether a skilled artisan can modify the non-conservative residues/sequences of the mouse and human IL-18, and generate the IL-18 sequence variants which maintain the function of IL-18 by conventional methods, rather, the issue is that the *claimed invention encompasses functional equivalents which are not required to have any structural similarity to the disclosed IL-18 sequences.* The specification provides no clear direction or enough guidance to teach how to make a commensurate number of such species with the desired biological property, nor written description of functional equivalents with significant structural dissimilarity. Based upon the very limited number of disclosed species, and a single type of amino acid substitution, it is not predictable what essential structures are required for the protein to be functional, and it would require undue experimentation to determine such. And the disclosure does not convey to those skilled in the art that the inventors were in possession of the genera of IL-18, variants or functional equivalents of IL-18 at the time the application was filed.

Rejections Over Prior Art:

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

Claims 1-6, and 8-10 remain rejected under 35 U.S.C. 102(a) as being anticipated by Ushio et al., EP 0 712 931 A2, for the reasons cited in the last Office Action, paper No. 12, at pages 7-8.

Applicants argument in paper No. 14 has been fully considered, but is not deemed persuasive for reasons below.

At page 8 of the response, the applicant argues that the prior art reference did not disclose an osteoclastgenic inhibiting activity of IL-18 and a functional equivalent thereof, that it is the applicants new finding that IL-18 and a functional equivalent thereof is useful as an osteoclastgenic inhibitory agent for treating and/or preventing osteoclast-related diseases, and the claimed invention involves industrial usefulness as pharmaceutical (the first paragraph), and that the present invention had much influence on the field of the art by disclose *a new use* of IL-18 and a functional equivalent thereof (the second paragraph). This argument is not persuasive because an intended use of a known composition does not alter the nature of the composition, and therefore, does not render the composition novel. Thus, the disclosed new use of IL-18 in the present application adds no patentable weight to the instant claims as they are directed to the composition of IL-18, which is anticipated by the prior art reference, as Ushio teaches the amino acid sequences of IL-18, as well as the industrial usefulness thereof as pharmaceutical in the treatment and/or prevention of the susceptive diseases (page 11, line 50 to page 12, line 22).

Claims 1-3, 6, and 8 also remain rejected under 35 U.S.C. 102(e) as being anticipated by Okamura et al., US 5,912,324, for the reasons cited in the last Office Action, paper No. 12, at page 8, and for the same reasons above, as the traversal is on the same ground as that above.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

Claim 28 is rejected under 35 U.S.C. 103(a) as being unpatentable over Ushio et al., EP 0 712 931 A2, or Okamura et al., US 5,912,324 as applied to the claims above, and further in view of Mark et al., US 4,588,585.

The teachings of Ushio and Okamura are reviewed above. Neither Ushio nor Okamura teaches Cys residue replacement in the amino acid sequence of human IL-18 (SEQ ID NO:6).

Mark teaches that biologically active proteins may contain cysteine residues that are nonessential to their activity but are free to form undesirable intermolecular or intramolecular links (column 1, lines 22-26), and that it would be desirable to alter the proteins in a manner that does not affect their activity adversely but reduces or eliminates their ability to form intermolecular or intramolecular links that cause the protein to adopt an undesirable tertiary structure (column 1, lines 41-50). The reference further teaches a synthetic mutein of a biologically active protein which has at least one of such cysteine residues deleted or replaced by

another amino acid (column 2, lines 13-18, and claim 2), and a method for making said synthetic mutein (column 2, lines 38-56).

It would have been obvious to the person of ordinary skill in the art at the time the invention was made to make a mutein of human IL-18 with one or more cysteine residues replaced, based on the amino acid sequence taught by Ushio and Okamura, using the method taught by Mark because of the desirable advantage suggested by Mark. The person of ordinary skill in the art would have been motivated to do so because of the therapeutic value of the IL-18 as taught by Ushio, and reasonably would have expected success because Mark has exemplified as regards such muteins of IFN-b and IL-2, and indicated that the teachings apply to any other biologically active protein that contains a functionally nonessential cysteine (column 3, lines 49-54).

Conclusion:

No claim is allowed.

Advisory Information:

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication should be directed to Dong Jiang whose telephone number is 703-305-1345. The examiner can normally be reached on Monday - Friday from 9:00 AM to 6:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler, can be reached on (703) 308-6564. The fax phone number for the organization where this application or proceeding is assigned is 703-308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Lorraine Spector

LORRAINE SPECTOR
PRIMARY EXAMINER

DJ
3/19/02